

Application No. 10/683,756  
Amendment dated December 14, 2006

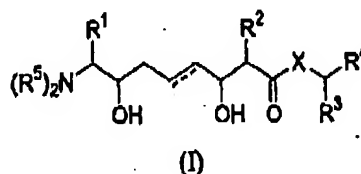
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### AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior listings of claims in the application.

1. (currently amended) A compound of the formula (I):



wherein,

each  $R^1$ ,  $R^2$ , and  $R^3$  are independently alkyl substituted with aryl or heteroaryl, each of which is optionally substituted with 1-5 substituents selected from  $OR^6$ , CN,  $NO_2$ ,  $NHR^7$ ,  $N(R^7)_2$ , halo,  $CONHR^7$ ,  $CON(R^7)_2$ ,  $CO_2R^8$ , or  $C_{1-6}$  alkyl;

X is N, O, or S;

$R^4$  is H,  $CON(R^7)_2$ ,  $CONHR^7$ ,  $CH_2OH$ ,  $CH(OH)CH=CH_2$ , or  $C(O)NHCHR^{10}CO_2H$ ;

each  $R^5$  is independently H, alkyl, alkenyl, aryl, heteroaryl, acyl,  $P^1$ , or  $C(O)CHR^{10}NH_2$ ;

each  $R^6$  is independently H, alkyl, or  $P^3$ ;

each  $R^7$  is independently H, alkyl, acyl, or  $P^2$ ;

each  $R^8$  is independently H, alkyl, aralkyl, or heteroaralkyl;

each  $R^{10}$  is independently an amino acid side chain;

each  $P^1$  and  $P^2$  is independently a nitrogen protecting group; and

each  $P^3$  is independently an oxygen protecting group;

or pharmaceutically acceptable salts thereof.

2. (currently amended) The compound of claim 1, wherein:

X is N or O;

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$R^1$  is alkyl substituted with aryl, which is optionally substituted with 1-5 substituents selected from  $OR^6$ , CN,  $NO_2$ ,  $NHR^7$ ,  $N(R^7)_2$ , halo,  $CONHR^7$ ,  $CON(R^7)_2$ ,  $CO_2R^8$ , or  $C_{1-6}$  alkyl;

$R^4$  is H,  $CON(R^7)_2$ ,  $C(O)NHCHR^{10}CO_2H$ , or  $CH_2OH$ ;

each  $R^5$  is independently H, alkyl, acyl,  $P^1$ , or  $C(O)CHR^{10}NH_2$ ;

each  $R^6$  is independently H, alkyl, or  $P^3$ ;

each  $R^7$  is independently H, alkyl, acyl, or  $P^2$ ;

each  $R^8$  is independently H, alkyl, aralkyl, or heteroaralkyl;

each  $R^{10}$  is independently an amino acid side chain;

each  $P^1$  and  $P^2$  is independently a nitrogen protecting group; and

each  $P^3$  is independently an oxygen protecting group.

3. (currently amended) The compound of claim 1, wherein:

$X$  is  $N$  or  $O$ ;

$R^1$  is alkyl substituted with aryl, which is optionally substituted with 1-5 substituents selected from  $OR^6$ , CN,  $NO_2$ , halo, or  $C_{1-6}$  alkyl;

$R^4$  is H,  $CONHR^7$ , or  $CH_2OH$ ;

each  $R^5$  is independently H or alkyl;

each  $R^6$  is independently H or alkyl;

$R^7$  is H, alkyl, or  $P^2$ ; and

$P^2$  is a nitrogen protecting group.

4. (currently amended) The compound of claim 1, wherein:

$X$  is  $N$  or  $O$ ;

$R^1$  is alkyl substituted with aryl, which is optionally substituted with 1-5 substituents selected from OH or  $C_{1-6}$  alkyl; and

$R_4$  is H,  $CONH_2$ , or  $CH_2OH$ .

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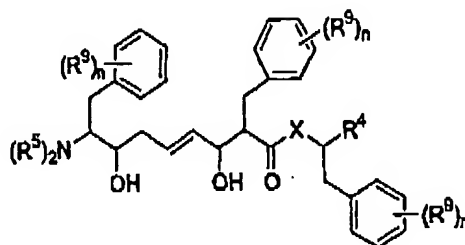
5. (currently amended) The compound of claim 1, wherein:

X is N or O;

R<sup>1</sup> is C<sub>1</sub> alkyl substituted with phenyl, which is substituted at the 2- and 6- positions with Me and is substituted at the 4- position with OH; and

R<sup>4</sup> is H, CONH<sub>2</sub>, or CH<sub>2</sub>OH.

6. (currently amended) The compound of claim 1 having the formula (II):



(II)

wherein,

X is N or O;

R<sup>4</sup> is H, CON(R<sup>7</sup>)<sub>2</sub>, CONHR<sup>7</sup>, CH<sub>2</sub>OH, or C(O)NHCHR<sup>10</sup>CO<sub>2</sub>H;

each R<sup>5</sup> is independently H, alkyl, acyl, P<sup>1</sup>, or C(O)CH(R<sup>10</sup>)NH<sub>2</sub>;

each R<sup>6</sup> is independently H, alkyl, or P<sup>3</sup>;

each R<sup>7</sup> is independently H, alkyl, acyl, or P<sup>2</sup>;

each R<sup>8</sup> is independently H, alkyl, aralkyl, or heteroaralkyl;

each R<sup>9</sup> is independently OR<sup>6</sup>, CN, NO<sub>2</sub>, NHR<sup>7</sup>, N(R<sup>7</sup>)<sub>2</sub>, halo, CONHR<sup>7</sup>, CON(R<sup>7</sup>)<sub>2</sub>, CO<sub>2</sub>R<sup>8</sup>, or C<sub>1-6</sub> alkyl;

each R<sup>10</sup> is independently an amino acid side chain;

each n is independently 0, 1, 2, 3, 4, or 5;

each P<sup>1</sup> and P<sup>2</sup> is independently a nitrogen protecting group; and

each P<sup>3</sup> is independently an oxygen protecting group.

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7. (original) The compound of claim 6, wherein:

$R^4$  is H,  $\text{CON}(R^7)_2$ ,  $\text{CONHR}^7$ , or  $\text{CH}_2\text{OH}$ ;  
each  $R^5$  is independently H, alkyl, or acyl;  
each  $R^6$  is independently H or alkyl;  
each  $R^7$  is independently H or alkyl;  
each  $R^9$  is independently  $\text{OR}^6$ , CN,  $\text{NO}_2$ , halo, or  $\text{C}_{1-6}$  alkyl; and  
each n is independently 0, 1, 2, or 3.

8. (original) The compound of claim 6, wherein:

$P^1$  is a BOC or Fmoc;  
 $P^2$  is a solid support; and  
 $P^3$  is *t*-Bu, Bn, Me, or Ac.

9. (original) The compound of claim 6, wherein:

$R^4$  is H,  $\text{CON}(R^7)_2$ ,  $\text{CONHR}^7$ , or  $\text{CH}_2\text{OH}$ ;  
each  $R^5$  is independently H, alkyl, acyl, or  $P^1$ ;  
each  $R^6$  is independently H or  $P^3$ ;  
each  $R^7$  is independently H or  $P^2$ ;  
each  $R^9$  is independently  $\text{OR}^6$  or  $\text{C}_{1-6}$  alkyl;  
each n is independently 0, 1, or 2;  
 $P^1$  is a BOC;  
 $P^2$  is a solid support; and  
 $P^3$  is *t*-Bu.

10. (original) The compound of claim 6, wherein:

$R^4$  is H,  $\text{CONH}_2$ , or  $\text{CH}_2\text{OH}$ ;  
each  $R^5$  is independently H,  $P^1$ , or  $\text{C}(\text{O})\text{CHR}^{10}\text{NH}_2$ ;  
each  $R^6$  is H or alkyl

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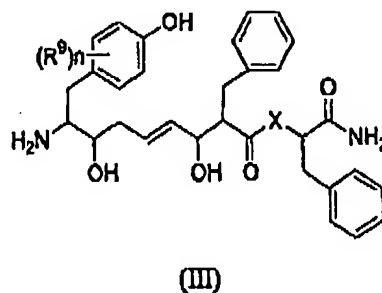
each  $R^9$  is  $C_{1-6}$  alkyl or  $OR^6$ ;

each  $R^{10}$  is independently an amino acid side chain;

each  $n$  is independently 1, 2, or 3; and

$P^1$  is a nitrogen protecting group.

11. (currently amended) The compound of claim 1 that is formula (III):



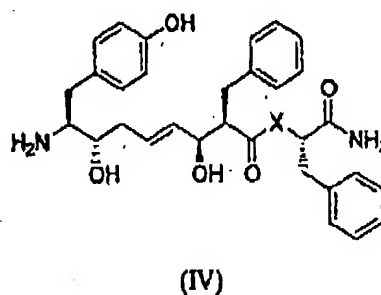
wherein,

X is  $\Theta$  or N;

$R^9$  is  $C_{1-6}$  alkyl; and

$n$  is 2.

12. (currently amended) The compound of claim 1 that is formula (IV):



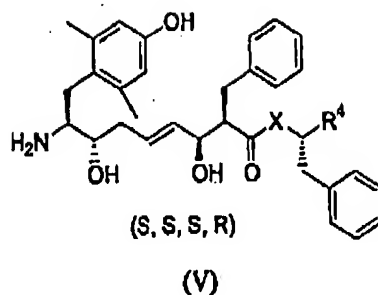
wherein X is N or  $\Theta$ .

13. (currently amended) The compound of claim 1 having the formula (V):

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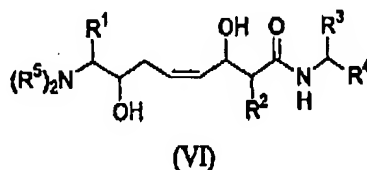


wherein

X is N or O; and

R<sup>4</sup> is CONH<sub>2</sub>, H, or CH<sub>2</sub>OH.

14. (original) The compound of claim 1 having the formula (VI):



wherein,

each R<sup>1</sup>, R<sup>2</sup>, and R<sup>3</sup> is independently alkyl substituted with aryl or heteroaryl, each of which is optionally substituted with 1-5 substituents selected from OR<sup>6</sup>, CN, NO<sub>2</sub>, NHR<sup>7</sup>, N(R<sup>7</sup>)<sub>2</sub>, halo, CONHR<sup>7</sup>, CON(R<sup>7</sup>)<sub>2</sub>, CO<sub>2</sub>R<sup>8</sup>, or C<sub>1-6</sub> alkyl;

R<sup>4</sup> is H, CON(R<sup>7</sup>)<sub>2</sub>, CONHR<sup>7</sup>, CH<sub>2</sub>OH, or CH(OH)CH=CH<sub>2</sub>, or C(O)NHCH<sub>2</sub>CH<sub>2</sub>CO<sub>2</sub>H;

each R<sup>5</sup> is independently H, alkyl, alkene, aryl, heteroaryl, acyl, or P<sup>1</sup>, or C(O)CH<sub>2</sub>CH<sub>2</sub>NH<sub>2</sub>;

each R<sup>6</sup> is independently H, alkyl, or P<sup>3</sup>;

each R<sup>7</sup> is independently H, alkyl, acyl, or P<sup>2</sup>;

each R<sup>8</sup> is independently H, alkyl, aralkyl, or heteroaralkyl;

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each  $R^{10}$  is independently an amino acid side chain;

each  $P^1$  and  $P^2$  is independently a nitrogen protecting group; and

each  $P^3$  is independently an oxygen protecting group.

15. (original) The compound of claim 14, wherein:

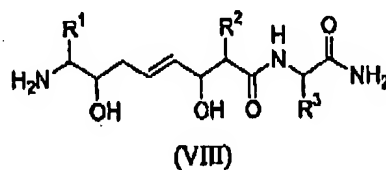
each  $R^1$ ,  $R^2$ , and  $R^3$  is independently alkyl substituted with aryl, each of which is optionally substituted with 1-5 substituents selected from  $OR^6$ , CN,  $NO_2$ , halo, or  $C_{1-6}$  alkyl;

$R^4$  is H,  $CON(R^7)_2$ , or  $CONHR^7$ , or  $C(O)NHCHR^{10}CO_2H$ ;

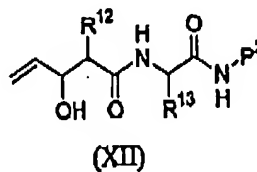
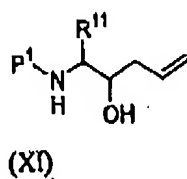
each  $R^5$  is independently H, alkyl, acyl,  $P^1$ , or  $C(O)CHR^{10}NH_2$ ; and

each  $R^{10}$  is independently an amino acid side chain.

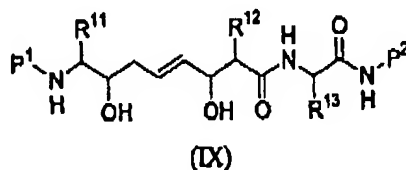
16. (original) A method of making a compound of the formula (VIII):



comprising coupling compounds of the formulas (XI) and (XII)



using a ruthenium catalyst, to give a compound of formula (IX); and



reacting the compound of formula (IX) with a deprotecting agent to give a compound of the formula (VIII);

wherein,

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each  $R^1$ ,  $R^2$ , and  $R^3$  is independently alkyl substituted with aryl or heteroaryl, each of which is optionally substituted with 1-5 substituents selected from  $OR^6$ , CN,  $NO_2$ ,  $NHR^7$ ,  $N(R^7)_2$ , halo,  $CONHR^7$ ,  $CON(R^7)_2$ ,  $CO_2R^8$ , or  $C_{1-6}$  alkyl;

each  $R^6$  is independently H, alkyl, or  $P^3$ ;

each  $R^7$  is independently H, alkyl, acyl, or  $P^4$ ;

each  $R^8$  is independently H, alkyl, aralkyl, or heteroaralkyl;

each  $R^{11}$ ,  $R^{12}$ , and  $R^{13}$  is independently alkyl substituted with aryl or heteroaryl, each of which is optionally substituted with 1-5 substituents selected from  $OR^{16}$ , CN,  $NO_2$ ,  $NHR^{17}$ ,  $N(R^{17})_2$ , halo,  $CONHR^{17}$ ,  $CON(R^{17})_2$ ,  $CO_2R^{18}$ , or  $C_{1-6}$  alkyl;

each  $R^{16}$  is independently H, alkyl, or  $P^3$ ;

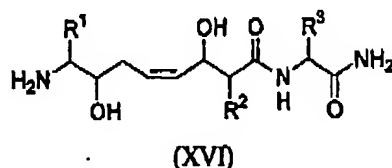
each  $R^{17}$  is independently H, alkyl, acyl, or  $P^4$ ;

each  $R^{18}$  is independently H, alkyl, aralkyl, or heteroaralkyl;

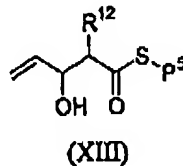
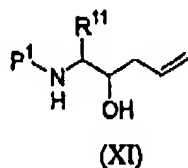
each  $P^1$ ,  $P^2$ , and  $P^4$  is independently a nitrogen protecting group; and

each  $P^3$  is independently an oxygen protecting group.

17. (original) A method of making a compound of the formula (XVI):



comprising coupling compounds of the formulas (XI) and (XIII)



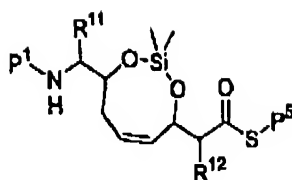
by first reacting the free alcohols with a silicon protecting group, and then treating the resulting compound with a ruthenium catalyst, giving a compound of the formula (VII);



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(VII)

reacting the compound of formula (VII) under pH conditions sufficient to remove acid labile protecting groups, if any;

treating the resulting product with peroxide and base under conditions sufficient to hydrolyze the thioester; and

coupling the resulting product with a solid phase peptide, giving a compound of the formula (XVI);

wherein,

each R<sup>1</sup>, R<sup>2</sup>, and R<sup>3</sup> is independently alkyl substituted with aryl or heteroaryl, each of which is optionally substituted with 1-5 substituents selected from OR<sup>6</sup>, CN, NO<sub>2</sub>, NHR<sup>7</sup>, N(R<sup>7</sup>)<sub>2</sub>, halo, CONHR<sup>7</sup>, CON(R<sup>7</sup>)<sub>2</sub>, CO<sub>2</sub>R<sup>8</sup>, or C<sub>1-6</sub> alkyl;

each R<sup>6</sup> is independently H, alkyl, or P<sup>3</sup>;

each R<sup>7</sup> is independently H, alkyl, acyl, or P<sup>4</sup>;

each R<sup>8</sup> is independently H, alkyl, aralkyl, or heteroaralkyl;

each R<sup>11</sup> and R<sup>12</sup> is independently alkyl substituted with aryl or heteroaryl, each of which is optionally substituted with 1-5 substituents selected from OR<sup>16</sup>, CN, NO<sub>2</sub>, NHR<sup>17</sup>, N(R<sup>17</sup>)<sub>2</sub>, halo, CONHR<sup>17</sup>, CON(R<sup>17</sup>)<sub>2</sub>, CO<sub>2</sub>R<sup>18</sup>, or C<sub>1-6</sub> alkyl;

each R<sup>16</sup> is independently H, alkyl, or P<sup>3</sup>;

each R<sup>17</sup> is independently H, alkyl, acyl, or P<sup>4</sup>;

each R<sup>18</sup> is independently H, alkyl, aralkyl, or heteroaralkyl;

each P<sup>1</sup> and P<sup>4</sup> is independently a nitrogen protecting group; and

each P<sup>3</sup> is independently an oxygen protecting group; and

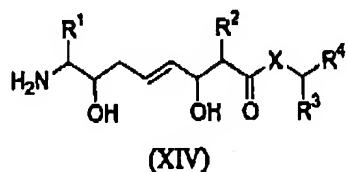
P<sup>5</sup> is a sulfur protecting group.

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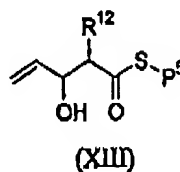
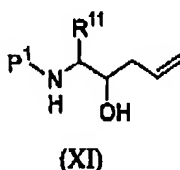
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18. (currently amended) A method of making a compound of the formula (XIV):



comprising coupling compounds of formulas (XI) and (XIII),



with a ruthenium catalyst;

treating the resulting compound with peroxide and base under conditions sufficient to hydrolyze the thioester;

amidation or esterification of the resulting acid; and

treatment of the resulting compound with a deprotecting agent sufficient to remove protecting groups, giving a compound of the formula (XIV);

wherein,

each  $R^1$ ,  $R^2$ , and  $R^3$  is independently alkyl substituted with aryl or heteroaryl, each of which is optionally substituted with 1-5 substituents selected from  $OR^6$ ,  $CN$ ,  $NO_2$ ,  $NHR^7$ ,  $N(R^7)_2$ , halo,  $CONHR^7$ ,  $CON(R^7)_2$ ,  $CO_2R^8$ , or  $C_{1-6}$  alkyl;

$X$  is  $N$  or  $O$ ;

$R^4$  is  $H$ ,  $CON(R^7)_2$ ,  $CONHR^7$ ,  $CH_2OH$ , or  $CH(OH)CH=CH_2$ ;

each  $R^6$  is independently  $H$ , alkyl, or  $P^3$ ;

each  $R^7$  is independently  $H$ , alkyl, acyl, or  $P^4$ ;

each  $R^8$  is independently  $H$ , alkyl, aralkyl, or heteroaralkyl;

each  $R^{11}$  and  $R^{12}$  are independently alkyl substituted with aryl or heteroaryl, each of

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which is optionally substituted with 1-5 substituents selected from  $\text{OR}^{16}$ ,  $\text{CN}$ ,  $\text{NO}_2$ ,  $\text{NHR}^{17}$ ,  $\text{N(R}^{17})_2$ , halo,  $\text{CONHR}^{17}$ ,  $\text{CON(R}^{17})_2$ ,  $\text{CO}_2\text{R}^{18}$ , or  $\text{C}_{1-6}$  alkyl;

each  $\text{R}^{16}$  is independently H, alkyl, or  $\text{P}^3$ ;

each  $\text{R}^{17}$  is independently H, alkyl, acyl, or  $\text{P}^4$ ;

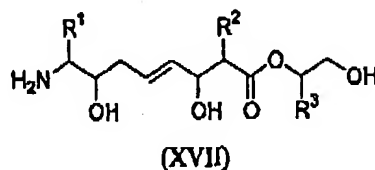
each  $\text{R}^{18}$  is independently H, alkyl, aralkyl, or heteroaralkyl;

each  $\text{P}^1$  and  $\text{P}^4$  is independently a nitrogen protecting group;

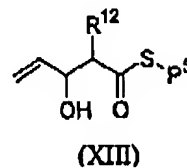
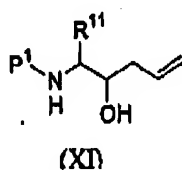
each  $\text{P}^3$  is independently an oxygen protecting group; and

$\text{P}^5$  is a sulfur protecting group.

19. (original) A method of making a compound of formula (XVII):



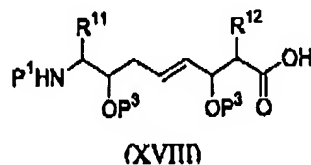
comprising coupling compounds of formulas (XI) and (XIII)



with a ruthenium catalyst;

treating the resulting compound with peroxide and base under conditions sufficient to hydrolyze the thioester; and

reacting the free hydroxyls with an oxygen protecting group to give a compound of formula (XVIII)



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coupling the compound of formula (XVIII) with an alcohol of formula  $R^{13}(\text{CHOH})\text{CHOR}^{16}$ ; and

treating the resulting compound with a deprotecting agent sufficient to remove protecting groups to give a compound of formula (XVII);

wherein,

each  $R^1$ ,  $R^2$ , and  $R^3$  is independently alkyl substituted with aryl or heteroaryl, each of which is optionally substituted with 1-5 substituents selected from  $\text{OR}^6$ , CN,  $\text{NO}_2$ ,  $\text{NHR}^7$ ,  $\text{N}(\text{R}^7)_2$ , halo,  $\text{CONHR}^7$ ,  $\text{CON}(\text{R}^7)_2$ ,  $\text{CO}_2\text{R}^8$ , or  $\text{C}_{1-6}$  alkyl;

each  $R^6$  is independently H, alkyl, or  $\text{P}^3$ ;

each  $R^7$  is independently H, alkyl, acyl, or  $\text{P}^4$ ;

each  $R^8$  is independently H, alkyl, aralkyl, or heteroaralkyl;

each  $R^{11}$ ,  $R^{12}$ , and  $R^{13}$  is independently alkyl substituted with aryl or heteroaryl, each of which is optionally substituted with 1-5 substituents selected from  $\text{OR}^{16}$ , CN,  $\text{NO}_2$ ,  $\text{NHR}^{17}$ ,  $\text{N}(\text{R}^{17})_2$ , halo,  $\text{CONHR}^{17}$ ,  $\text{CON}(\text{R}^{17})_2$ ,  $\text{CO}_2\text{R}^{18}$ , or  $\text{C}_{1-6}$  alkyl;

each  $R^{16}$  is independently H, alkyl, or  $\text{P}^3$ ;

each  $R^{17}$  is independently H, alkyl, acyl, or  $\text{P}^4$ ;

each  $R^{18}$  is independently H, alkyl, aralkyl, or heteroaralkyl;

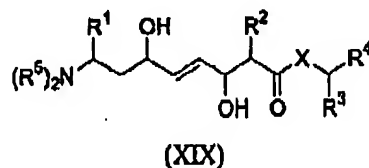
each  $\text{P}^1$  and  $\text{P}^4$  is independently a nitrogen protecting group;

each  $\text{P}^3$  is independently an oxygen protecting group; and

$\text{P}^5$  is a sulfur protecting group.

20. (original) A composition comprising a compound of formula (I) in claim 1 and a pharmaceutically acceptable carrier.

21. (currently amended) A compound of formula (XIX):



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wherein,

each  $R^1$ ,  $R^2$ , and  $R^3$  is independently alkyl substituted with aryl or heteroaryl, each of which is optionally substituted with 1-5 substituents selected from  $OR^6$ , CN,  $NO_2$ ,  $NIIR^7$ ,  $N(R^7)_2$ , halo,  $CONHR^7$ ,  $CON(R^7)_2$ ,  $CO_2R^8$ , or  $C_{1-6}$  alkyl;

X is N, ~~O~~, or S;

$R^4$  is H,  $CON(R^7)_2$ ,  $CONHR^7$ ,  $CH_2OH$ ,  $CH(OH)CH=CH_2$ , or  $C(O)NHCHR^{10}CO_2H$ ;

each  $R^5$  is independently H, alkyl, alkenyl, aryl, heteroaryl, acyl,  $P^1$ , or  $C(O)CHR^{10}NH_2$ ;

each  $R^6$  is independently H, alkyl, or  $P^3$ ;

each  $R^7$  is independently H, alkyl, acyl, or  $P^2$ ;

each  $R^8$  is independently H, alkyl, aralkyl, or heteroaralkyl;

each  $R^{10}$  is independently an amino acid side chain;

each  $P^1$  and  $P^2$  is independently a nitrogen protecting group;

each  $P^3$  is independently an oxygen protecting group; and

or pharmaceutically acceptable salts thereof.

22. (currently amended) The compound of claim 21 wherein:

X is N or ~~O~~;

$R^1$  is alkyl substituted with aryl, which is optionally substituted with 1-5 substituents selected from  $OR^6$ , CN,  $NO_2$ ,  $NIIR^7$ ,  $N(R^7)_2$ , halo,  $CONHR^7$ ,  $CON(R^7)_2$ ,  $CO_2R^8$ , or  $C_{1-6}$  alkyl;

$R^4$  is H,  $CON(R^7)_2$ ,  $C(O)NHCHR^{10}CO_2H$ , or  $CH_2OH$ ; and

each  $R^5$  is independently H, alkyl, acyl,  $P^1$ , or  $C(O)CHR^{10}NH_2$ ;

each  $R^{10}$  is independently an amino acid side chain.

23. (currently amended) The compound of claim 21, wherein:

X is N or ~~O~~;

$R^1$  is alkyl substituted with aryl, which is optionally substituted with 1-5 substituents selected from  $OR^6$ , CN,  $NO_2$ , halo, or  $C_{1-6}$  alkyl;

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$R^4$  is H,  $\text{CONHR}^7$ , or  $\text{CH}_2\text{OH}$ ;

each  $R^5$  is independently H or alkyl;

each  $R^6$  is independently H or alkyl; and

$R^7$  is H, alkyl, or  $\text{P}^2$ .

24. (currently amended) The compound of claim 21, wherein:

X is N or  $\text{O}^-$ ;

$R^1$  is alkyl substituted with aryl, which is optionally substituted with 1-5 substituents selected from OH or  $\text{C}_{1-6}$  alkyl; and

$R^4$  is H,  $\text{CONH}_2$ , or  $\text{CH}_2\text{OH}$ .

25. (currently amended) The compound of claim 21, wherein:

X is N or  $\text{O}^-$ ;

$R^1$  is  $\text{C}_1$  alkyl substituted with phenyl, which is substituted at the 2- and 6- positions with Me and is substituted at the 4- position with OH; and

$R^4$  is H,  $\text{CONH}_2$ , or  $\text{CH}_2\text{OH}$ .

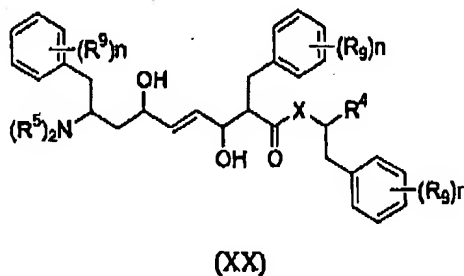
26. (original) The compound of claim 21, wherein

X is N;

$R^1$  is methyl substituted with phenyl, which is substituted at the 4- position with OH; and

$R^4$  is  $\text{CONH}_2$ .

27. (currently amended) The compound of claim 21 having the formula (XX):



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X is N or O;

$R^4$  is H,  $\text{CON}(R^7)_2$ ,  $\text{CONHR}^7$ ,  $\text{CH}_2\text{OH}$ , or  $\text{C}(\text{O})\text{NHCHR}^{10}\text{CO}_2\text{H}$ ;

each  $R^5$  is independently H, alkyl, acyl,  $P^1$ , or  $\text{C}(\text{O})\text{CHR}^{10}\text{NH}_2$ ;

each  $R^6$  is independently H, alkyl, or  $P^3$ ;

each  $R^7$  is independently H, alkyl, acyl, or  $P^2$ ;

each  $R^8$  is independently H, alkyl, aralkyl, or heteroaralkyl;

each  $R^9$  is independently  $\text{OR}^6$ , CN,  $\text{NO}_2$ ,  $\text{NHR}^7$ ,  $\text{N}(R^7)_2$ , halo,  $\text{CONHR}^7$ ,  $\text{CON}(R^7)_2$ ,  $\text{CO}_2R^8$ , or  $\text{C}_{1-6}$  alkyl;

each  $R^{10}$  is independently an amino acid side chain;

each n is independently 0, 1, 2, 3, 4, or 5;

each  $P^1$  and  $P^2$  is independently a nitrogen protecting group; and

each  $P^3$  is independently an oxygen protecting group.

28. (original) The compound of claim 27, wherein:

$R^4$  is H,  $\text{CON}(R^7)_2$ ,  $\text{CONHR}^7$ , or  $\text{CH}_2\text{OH}$ ;

each  $R^5$  is independently H, alkyl, or acyl;

each  $R^6$  is independently H or alkyl;

each  $R^7$  is independently H or alkyl;

each  $R^9$  is independently  $\text{OR}^6$ , CN,  $\text{NO}_2$ , halo, or  $\text{C}_{1-6}$  alkyl; and

each n is independently 0, 1, 2, or 3.

29. (original) The compound of claim 27, wherein:

$R^4$  is H,  $\text{CON}(R^7)_2$ ,  $\text{CONHR}^7$ , or  $\text{CH}_2\text{OH}$ ;

each  $R^5$  is independently H, alkyl, acyl, or  $P^1$ ;

each  $R^6$  is independently H or  $P^3$ ;

each  $R^7$  is independently H or  $P^2$ ;

each  $R^9$  is independently  $\text{OR}^6$  or  $\text{C}_{1-6}$  alkyl;

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each  $n$  is independently 0 or 1;

$P^1$  is a BOC;

$P^2$  is a solid support; and

$P^3$  is *t*-Bu.

30. (original) The compound of claim 27, wherein:

$R^4$  is H,  $\text{CONH}_2$ , or  $\text{CH}_2\text{OH}$ ;

each  $R^5$  is independently H,  $P^1$ , or  $\text{C}(\text{O})\text{CHR}^{10}\text{NH}_2$ ;

each  $R^6$  is H or alkyl

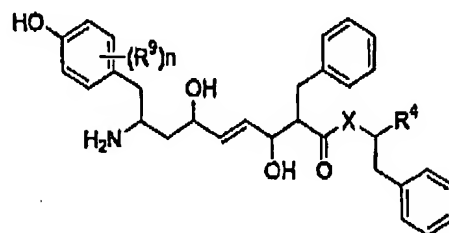
each  $R^9$  is  $\text{C}_{1-6}$  alkyl or  $\text{OR}^6$ ;

each  $R^{10}$  is independently an amino acid side chain;

each  $n$  is independently 1, 2, or 3; and

$P^1$  is a nitrogen protecting group.

31. (currently amended) The compound of claim 21 having the formula (XXI):



(XXI)

wherein,

$X$  is  $\text{O}$  or  $\text{N}$ ;

$R^4$  is H,  $\text{CONH}_2$ , or  $\text{CH}_2\text{OH}$ ;

$R^9$  is  $\text{C}_{1-6}$  alkyl; and

$n$  is 2.

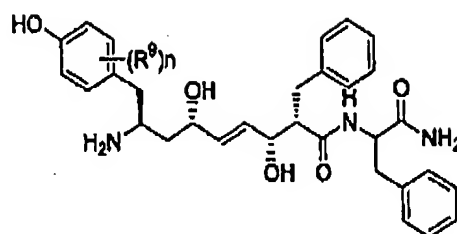
32. (original) The compound of claim 21 having the formula (XXII):



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(S, S, R, S)

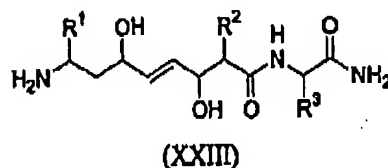
(XXII)

wherein

$R^2$  is  $C_{1-6}$  alkyl; and

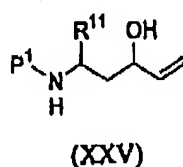
$n$  is 0, 1, or 2.

33. (original) A method of making a compound of formula (XXIII);

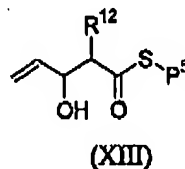


(XXIII)

comprising coupling compounds of formulas (XXV) and (XIII)



(XXV)



(XIII)

using a ruthenium catalyst, giving a compound of the formula (XXIV);

treating the resulting product with peroxide and base under conditions sufficient to hydrolyze the thioester;

coupling the resulting product with a solid phase peptide; and

treating the resulting compound with a deprotecting agent, giving a compound of the formula (XXIII);

wherein,

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each  $R^1$ ,  $R^2$ , and  $R^3$  is independently alkyl substituted with aryl or heteroaryl, each of which is optionally substituted with 1-5 substituents selected from  $OR^6$ , CN,  $NO_2$ ,  $NHR^7$ ,  $N(R^7)_2$ , halo,  $CONHR^7$ ,  $CON(R^7)_2$ ,  $CO_2R^8$ , or  $C_{1-6}$  alkyl;

each  $R^6$  is independently H, alkyl, or  $P^3$ ;

each  $R^7$  is independently H, alkyl, acyl, or  $P^4$ ;

each  $R^8$  is independently H, alkyl, aralkyl, or heteroaralkyl;

each  $R^{11}$  and  $R^{12}$  is independently alkyl substituted with aryl or heteroaryl, each of which is optionally substituted with 1-5 substituents selected from  $OR^{16}$ , CN,  $NO_2$ ,  $NHR^{17}$ ,  $N(R^{17})_2$ , halo,  $CONHR^{17}$ ,  $CON(R^{17})_2$ ,  $CO_2R^{18}$ , or  $C_{1-6}$  alkyl;

each  $R^{16}$  is independently H, alkyl, or  $P^3$ ;

each  $R^{17}$  is independently H, alkyl, acyl, or  $P^4$ ;

each  $R^{18}$  is independently H, alkyl, aralkyl, or heteroaralkyl;

each  $P^1$  and  $P^4$  is independently a nitrogen protecting group;

each  $P^3$  is independently an oxygen protecting group; and

$P^5$  is a sulfur protecting group.

34. (original) A composition comprising a compound of formula (XIX) in claim 21 or pharmaceutically acceptable salts thereof and a pharmaceutically acceptable carrier.

35. (currently amended) A method of treating a mu opioid receptor (MOR) mediated disorder that is pain in a subject comprising administering a compound of formula (I) in claim 1 or a compound of formula (XIX) in claim 21 or pharmaceutically acceptable salts thereof.

36. (currently amended) A method of treating a mu opioid receptor (MOR) mediated disorder that is pain in a subject comprising administering a composition comprising a compound of formula (I) in claim 1 or a compound of formula (XIX) in claim 21 or pharmaceutically acceptable salts thereof.

37. (original) A method of treating pain in a subject, comprising administering to the subject a compound of formula (I) in claim 1 or of formula (XIX) in claim 21 or pharmaceutically acceptable salts thereof.

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38. (cancelled)